REMARKS

Claims 1, 2, 4-35 and 37-41 are pending in this application. Claims 2, 8, 14 and 32 have been withdrawn from consideration.

Rejection in view of Pacetti and Sheu

Claims 1,4-7, 9-13, 15-30, 33, 34 and 37-41 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Pacetti et al. US 6,663,662 (Pacetti) in view of Sheu et al. 5,837,377 (Sheu). Applicant respectfully traverses this rejection and its supporting remarks.

Pacetti discloses medical articles, which may be stents, which carry and release therapeutic substances. The stents *per se* are produced from stainless steel. See column 4, lines 57-59. There is no disclosure of ceramic substrates.

The substrate may contain depressions to serve as reservoirs for the therapeutic agent to be released; Figure 2A is exemplary. The compositions **26** filling the cavities or micropores **24** are compositions of therapeutic agent mixed with polymer. Col. 13 line 27, *et seq.* Over the cavities **24**, is disposed a diffusion barrier layer **28**. *Id.*

Pacetti, however, does not teach disposing a therapeutic agent composition within depressions beneath a *multilayer* coating region as claimed (the diffusion barrier layers **28** are of single layer thickness in Pacetti). Moreover, the diffusion barrier layer **28** of Pacetti is made from particle-containing polymeric materials, none of which are disclosed as polyelectrolytes.

In other words, Pacetti fails to disclose a polyelectrolyte-containing layer, much less a multilayer coating region comprising multiple polyelectrolyte layers as here claimed.

The Examiner acknowledges that Pacetti fails to disclose a plurality of polyelectrolyte layers covering the stent, and turns to Sheu to make up for this deficiency.

Sheu discloses medical articles, including contact lenses, having polyelectrolyte coatings for the purpose of rendering them hydrophilic. The article comprises a "substrate", an "ionic polymer layer" and a "disordered polyelectrolyte coating." The coating must include at least one infiltrating or intermixed polyelectrolyte. See, for example, column 1, line 59, to column 2, line 19. An example of what is meant by infiltrating is given at col. 8, lines 1-8, in which the polymeric layer is a hydrogel polymer or copolymer and the solvent system is chosen to cause the polymeric layer to swell, thereby allowing one or more polyelectrolytes to penetrate or infiltrate

the polymeric layer.

The polyelectrolyte coating of Sheu may contain charge-neutral molecules that enhance biocompatibility or molecules that are bioactive, such as heparin. See col. 1, line 66 to col. 2, line 1 and col. 7, lines 47-49. Sheu does not teach or suggest that the polyelectrolyte coating therein is useful to *control the release* of such bioactive molecules, much less bioactive molecules disposed *beneath* the polyelectrolyte coating. In fact, Sheu does not teach or suggest that the bioactive molecules are released at all. As noted above, Sheu discloses medical articles, including contact lenses, in which polyelectrolyte coatings are used for the purpose of rendering the medical articles hydrophilic—this application is remote from using coatings as diffusion barriers for underlying therapeutic agents as described in Pacetti.

With respect to the disordered polyelectrolyte coating of Sheu, although at least one polyelectrolyte must have a charge opposite to the ionic polymeric layer, see col. 1, lines 51-53, Sheu further teaches that two or more polyelectrolytes of different charge may be intermixed, see, e.g., col. 1, lines 59-61, which may render the polyelectrolyte coating and the ionic polymer layer of the same overall charge.

The differing nature of the polyelectrolyte coating of Sheu, the polymer layer of Pacetti and the polymer layers of the present claims is further illustrated at column 7, lines 31-33, of Sheu, where it is disclosed that, after drying, the substrate may be dip-coated with one or more additional polyelectrolyte or other solutions. Sheu further suggests that the charge of the additional solution is of no significance, noting that "[t]he additional solution may contain polyelectrolytes of the same or different charge sign."

With regard to present claims 12-18, ceramic substrates are broadly disclosed in Sheu ("substrate may be made of metal, ceramic, glass, composite or a polymer"), but there is no disclosure of any type article that could utilize a ceramic substrate.

Furthermore, there is no reason why one or ordinary skill in the art would make the articles of Pacetti more hydrophilic. *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___ (2007).

Accordingly, to arrive at the subject matter presently claimed would require, at the very least, undue hindsight of the type proscribed by precedent. See, merely for example, *Akzo N. V.* v. *U.S. International Trade Commission,* 808 F.2d 1241, 1480-81, 1 USPQ2d, 1241, 1246 (Fed. Cir. 1986), *cert. denied.* 482 U.S. 909 (1987), *Loctite Corp.* v. *Ultraseal Ltd.*, 781 F.2d 861, 874,

228 USPQ 90-99 (Fed. Cir. 1985). See also MPEP 2142, second paragraph.

The Examiner has taken the position that it would have been obvious to "modify the material property of the polymeric cover [barrier layer] of the Pacetti et al. reference with the water soluble multiple polymeric polyelectrolyte layers having different net charges in order to create a more versatile, biocompatible surface capable of being adsorbed by water."

The disordered polyelectrolyte coatings of Sheu, however, are not water soluble, but rather are said to form a durable hydrophobic coating, resistant to changes in pH, elevated temperatures, exposure to detergents or organic solvents, mechanical stress, abrasion, and repeated ultrasonic washings. See, col. 1, lines 19-24 and col. 3, lines 21-25.

Moreover, the layers of Sheu are not taught as being "adsorbed" by water.

Nor has the Examiner explained why the layers of Sheu are any more "versatile" than the layers of Pacetti (which may vary widely in composition), or why the layers of Sheu are any more "biocompatible" than the layers of Pacetti.

Furthermore, in Pacetti, the diffusion barrier layer is used to control the release rate of an active agent from the underlying polymer composition. The disordered polyelectrolyte coating of Sheu, on the other hand, is designed to ionically bond to an ionic polymeric layer and provide the articles of Sheu with a durable hydrophilicity. See Abstract, col. 1, lines 19-24 and col. 3, lines 21-25. If the device of Pacetti were modified in accordance with the teachings of Sheu, this would require the creation of an ionic polymeric layer over the diffusion barrier layer of Pacetti, and a disordered polyelectrolyte coating ionically bound to the ionic polymeric layer, which modification would be expected to interfere with, or even prevent, the controlled release of active agent as sought by Pacetti. See *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984).

Furthermore, in teaching that the "ionically bonded" hydrophilic coatings described in Sheu are durable (e.g., resistant to changes in pH, elevated temperatures, exposure to detergents or organic solvents, abrasion, repeated ultrasonic washings, etc.), Sheu teaches away from the *biodisintegrable* polyelectrolyte multilayer coating regions claimed in presently pending claims 4, 12, 13, 15-17, 20, 30 and 40.

A biodisintegrable polyelectrolyte multilayer coating region as claimed is beneficial in that one is left with a bare ceramic or metallic structure. As noted in paragraph [0004] of the

present invention, metallic and ceramic structures are robust, resulting in excellent resistance against mechanical damage. Moreover, they are frequently more biologically inert than polymers, and in some cases are bioactive. Furthermore, metallic and ceramic structures can be made porous, thereby enabling them to hold large amounts of drugs.

Finally, even with the use of hindsight, the combination of reference teachings would not result in the here-claimed invention. Neither of the references teaches a multilayer coating region in which *each* polyelectrolyte layer has a *net charge* opposite in sign from the adjacent layers as currently claimed. See above discussion of Sheu.

Thus, reconsideration and withdrawal of this rejection under 35 U.S.C. 103 are respectfully requested.

Rejection in view of Pacetti, Sheu and Anderson

Claim 31 as been rejected under 35 U.S.C. 103(a) as being unpatentable over Pacetti in view of Sheu and Anderson et al. US 2005/0172852 (Anderson). This rejection is respectfully traversed.

Claim 31 recites the additional limitation that "metal or metal oxide nanoparticles" are included in the "multilayer coating system." The Examiner has relied on Anderson as supplying the additional teaching to provide a *prima facie* case of obviousness.

Anderson discloses particles that are used in "variable appearance tissue markings." The particles may be nanoparticles. See paragraph [0037]. The coatings of the particles may be porous. See paragraph [0030]. The coatings may be a metal oxide, see paragraph [0029], and the particle may include "subparticles," see paragraphs [0032] and [0038]. However, the subparticles are *not* disclosed as causing the porosity to provide the motivation suggested by the Examiner. The relevance of the Anderson disclosure is not readily seen, even if the Examiner's description of it were correct. Without the hindsight afforded by the present disclosure, it is not seen why one of ordinary skill in the art would be motivated to include the particles of Anderson into the disordered polyelectrolyte coating described in Sheu, in order to create a multilayer coating region comprising multiple polyelectrolyte layers and further comprising metal or metal oxide nanoparticles, as claimed in claim 31.

More generally, the field of art of Anderson is completely different from those of Pacetti and Sheu. Thus, inclusion of Anderson in the prior art relied on to make out a *prima facie* case emphasizes the improper use of undue hindsight. *Wang Laboratories, Inc. v. Toshiba Corp.*, 993 F.2d 858, 26 USPQ2d 1767 (Fed. Cir. 1993), *In re Clay*, 966 F.2d 656, 23 USPQ 2d, 1058, 1060 (Fed. Cir. 1992), *King Instrument Corp. v. Otari Corp.* 767 F.2d 853, 226 USPQ. 402 (Fed. Cir. 1985).

Reconsideration and withdrawal of this rejection under 35 U.S.C. 103 are respectfully requested.

Rejection in view of Harish and Sheu

Claim 35 has been rejected under 35 U.S.C. 103(a) as being unpatentable over Harish et al. U.S. Patent No. 6,506,437 (Harish) in view of Sheu. This rejection is respectfully traversed.

Claim 35 recites a process for producing one embodiment within Applicants' invention generally.

Harish discloses a method for coating medical devices having a plurality of "depots." The depots are filled with a composition of polymer and therapeutic agent. The process is diagrammed in Figure 1. As can readily be seen from the figure, no matter which path is chosen, the result will be a composition containing a mixture of therapeutic agent and polymer filling the depots. Harish discloses that the weight percentage of therapeutic agent in the composition depends on a number of factors including the desired release characteristics. Column 6, lines 31-36. When there is a polymeric topcoat, the particulars of the topcoat also control release. Column 10, line 65 to column 11, line 9.

As the Examiner has acknowledged, Harish does not disclose "polyelectrolyte layers covering a stent." Sheu has been discussed above. For example, Applicant has, *inter alia*, noted above that Sheu does not teach or suggest that any therapeutic agents are released from the polyelectrolyte coating taught by Sheu. Applicant has also noted that Sheu does not teach or suggest that the polyelectrolyte coating is useful to control the release of any bioactive agents. Rather, Sheu discloses medical articles, including contact lenses, having polyelectrolyte coatings for the purpose of rendering them hydrophilic.

Furthermore, if the device of Harish were modified in accordance with the teachings of

Sheu, this would result in the creation of an ionic polymeric layer and a disordered polyelectrolyte coating, which structure is noted in Sheu to be very stable, and which would interfere with, even prevent, the controlled release of active agent as taught by Harish.

Thus, the reasons why there would be no suggestion in the references for taking the polyelectrolyte layer from Sheu and applying it to the device of Harish are analogous to those discussed above with respect to Pacetti. Moreover, the reasons why the references teach away from the invention are analogous to those above. In addition to the authorities cited above, *In re Baird*, 16 F.3d 380, 29 USPQ 2d 1550 (Fed. Cir. 1994), is relevant to the issue of the references teaching *away* from their combination. Also see MPEP 2141.02 VI and the cases cited therein.

With respect to the *method* aspects of claim 35, this claim requires a method that comprises (a) inserting a disintegrable material into said depressions to form filled depressions, (b) depositing polyelectrolyte layers over the filled depressions by a method comprising depositing a first polyelectrolyte layer having a first net charge over the substrate, depositing a second polyelectrolyte layer having a second net charge that is opposite in sign to the first net charge over the first polyelectrolyte layer, and depositing additional polyelectrolyte layers, each having a net charge that is opposite in sign to the preceding layer, (c) subsequently removing the disintegrable material from the depressions and (d) subsequently introducing said therapeutic agent into the depressions.

Thus, after the polyelectrolyte layer is applied in step (b), the disintegrable material that was placed in the depressions in step (a) is removed in step (c). Only then is the agent added to the depressions in step (d). No method of this nature is taught or suggested in Harish and/or Sheu.

For at least the above reasons, reconsideration and withdrawal of this rejection under 35 U.S.C. 103 are respectfully requested.

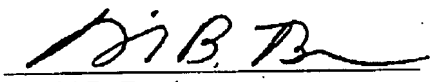
Conclusion

In view of the above, Applicant submits that the pending are in condition for allowance. If the Examiner believes there are still unresolved issues, a telephone call to the undersigned would be welcomed.

Serial No.: 10/805,576

All fees due and owing in respect to this Amendment may be charged to deposit account number 50-1047.

Respectfully submitted,



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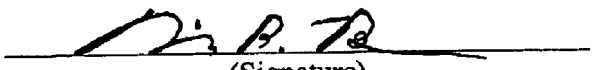

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